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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/526,372	03/03/2005	IWAO OHIZUMI	1254-0274PUS1	3366

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
07/30/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/526,372	OHIZUMI ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 6/11/07, is acknowledged.

2. Claims 1-9 and 12 are pending and under examination in the instant application.

3. In view of the amendment filed on 6/11/07, only the following rejections are remained.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 7-9 and 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 7 and 12 are indefinite because they recite amino acid sequence homology without providing a SEQ ID NO reference, it is unclear how the skilled artisan would find the correspondent of those amino acids. Finally, claims 7 and 12 recite "sequence homology is 90%/94% or higher", it is indefinite to compare amino acids between molecules without structural features for the comparison.

Applicant's arguments, filed 6/11/07, have been fully considered, but have not been found convincing.

Applicant directs the Examiner's attention to *Faulkner V Inglis*, 79 U.S.P.Q.2d 1001, 1008 (Fed. Cir. 2006), which state that "Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference (where permitted) of such genes and sequences".

However, *Faulkner V Inglis,* deals with written description issue. The issue at hand is that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Accordingly, *Faulkner V Inglis,* is irrelevant to the issue at hand.

Applicant further argues that a protein used to generate antibodies is an MRL/lpr mouse is not limited to any specific protein.

Again, the issue here is not written description or enablement, but indefiniteness of the claimed invention.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 7-9 and 12 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Pat. No. 6,235,714.

The `714 patent teaches six MRL/lpr mice were hyperimmunized with target antigen such as EGFR, TNFα, IL-1β among others (see fig. 19 and col., 8, under selection and preparation of CRAAs in particular) to drive the immune system to generate catalytic antibodies. Blood will be obtained from the retro-orbital plexus at ten day intervals (see col., 14, under immunization, col., 43, lines 56-66 in particular). Claims 10-12 are included because the target antigens listed in fig. 19, the antigen protein exhibits high amino acid sequence homology in a human and mouse, wherein the amino acid sequence homology is 90% or 94 % or higher in the absence of evidence to the contrary.

The reference teachings anticipate the claimed invention.

Applicant's arguments, filed 6/11/07, have been fully considered, but have not been found convincing.

Applicant points to the both the amendment of claim 7 which now recites, " a human antigen which has homology of 90% or more at the amino acid sequence level to a homolog protein of the nonhuman animal to be immunized" and to "Exhibit A" sequence alignment data showing the percentage homology between human and mouse EGFR, TNFα and IL-β. Applicant submits that these proteins are 78%, 87% and 78% homologous, respectively. Applicant concludes that all antigens to which antibodies were generated in Paul et al are lower than 90% homologous between human and mouse.

However, The `714 patent is not limited to EGFR, TNFα and IL-β as applicant argues. However, the human antigen in the exemplary CRAA-IL1-β peptide (PKKKMEK) (see fig. 16) shares 100% homology with the mouse peptide antigen (see Exhibit A, under amino acid positions in the "Query" 90-97). This human antigen reads on the claimed invention. Further, the `714 patent teaches other target antigens listed in fig. 19 such as CD4, HER2, Macrophage inhibitory factor, CD80, CD86, CD28, CD70, CD11b/CD18, CD23, ICAM-1, VLA-4, C5, IL-1 beta Receptor, GPIIb/IIIa receptor, FVII, PAI-1, IL-4, IL-4 receptor, IL-5, IL-5 receptor, IgE, Eotaxin, Eotaxin receptor, PDGF, PDGF beta receptor, αvβ3 integrin. Applicant fail to address the homology of said antigens. These antigen protein exhibits high amino acid sequence homology in a human and mouse, wherein the amino acid sequence homology is 90% or 94 % or higher in the absence of evidence to the contrary.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 7-9 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 872 488 A1 (IDS ref. No. BA) in view of Fu and Storb (Science, 297:2006-2008, 2002).

The EP `488 publication teach a method for producing an anti-Fas ligand antibody comprising a MPL. lpr/lpr mouse (nonhuman) animal with FAS function defects with an Fas ligand-expressed COS cells as an antigen (see p. 7, line 5-55 in particular). Claim 10 is included because the mouse Fas ligand is highly homologous to the human, 85%.

The claimed invention differs from the reference teachings only by the recitation that the human antigen which has homology of 90% or more at the amino acid sequence level to a homolog protein of the nonhuman animal to be immunized in claim 7, wherein the amino acid sequence homology is 94% or higher in claim12.

Fu and Storb teach autoreactive B cells that produce antibody against self-antigen are normally deleted through the Fas receptor/Fas ligand-mediated pathway of apoptosis. However, in mice deficient in either Fas receptor or Fas ligand, autoreactive B cells cannot be deleted. They do not accumulate in follicles but instead became trapped in side the T cell zone of lymphoid tissues, where they continue to proliferate and undergo somatic hypermutation, producing more autoantigody against self-antigen (see page 2007, col., 2, Figure legend). In MLR.Fas^{lpr} mice, autoreactive B cells expressing antiself antibodies spontaneously accumulated in the T cell-rich zone at the red pulp border of lymphoid tissues. The B lymphocytes underwent somatic hypermutation in this zone (page 2007, 1st col., 1st ¶ in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute Fas ligand taught by the EP `488 publication with the antigen protein which exhibits high amino acid sequence homology in a human and a mouse (self antigens) taught by Fu and Storb in a method for producing an antibody taught by the `488 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because in mice deficient in either Fas receptor or Fas ligand, autoreactive B cells cannot

be deleted. They do not accumulate in follicles but instead became trapped in side the T cell zone of lymphoid tissues, where they continue to proliferate and undergo somatic hypermutation, producing more autoantibody against self-antigen.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments, filed 6/11/07, have been fully considered, but have not been found convincing.

Applicants state that they will submit a verified English language translation of the priority document PCT/JP02/08998 to provide support that the effective filing date of the presently claimed invention is Sept. 4, 2002, which predate Fu et al reference teachings (Sept. 20, 2002).

However, the rejection will be maintained until the English language translation of the priority document is provided. It is incumbent upon the Applicant to provide the specific page number(s) of the priority document, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for in the priority document PCT/JP02/08998.

10. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 872 488 A1 (IDS ref. No. BA) in view of Fu and Storb (Science, 297:2006-2008, 2002) as applied to claims 7-9 and 12, above and further in view of Veugelers et al (J BC 274(33):26968-26977, 1999) for the same reasons set forth in the previous Office Action mailed 2/9/07.

Applicant's arguments, filed 6/11/07, have been fully considered, but have not been found convincing.

Applicants state that they will submit a verified English language translation of the priority document PCT/JP02/08998 to provide support that the effective filing date of the presently claimed invention is Sept. 4, 2002, which predate Fu et al reference teachings (Sept. 20, 2002).

However, the rejection will be maintained until the English language translation of the priority document is provided. It is incumbent upon the Applicant to provide the specific page number(s) of the priority document, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for in the priority document PCT/JP02/08998.

11. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 872 488 A1 (IDS ref. No. BA) in view of Fu and Storb (Science, 297:2006-2008, 2002) as applied to claims 7-9 and 12 above, and further in view of Veugelers et al (Trends in Glycosience and Glycotechnology, 10(52):145-152, 1998 for the same reasons set forth in the previous Office Action mailed 2/9/07.

Applicant's arguments, filed 6/11/07, have been fully considered, but have not been found convincing.

Applicants state that they will submit a verified English language translation of the priority document PCT/JP02/08998 to provide support that the effective filing date of the presently claimed invention is Sept. 4, 2002, which predate Fu et al reference teachings (Sept. 20, 2002).

However, the rejection will be maintained until the English language translation of the priority document is provided. It is incumbent upon the Applicant to provide the specific page number(s) of the priority document, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for in the priority document PCT/JP02/08998.

12. No claim is allowed.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

July 18, 2007

Maher Haddad

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